Loss of Surface Antigen in HIV/HBV Co-infected Individuals

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OPERA® The Longitudinal Cohort

Background

- Antiviral therapy is highly effective in suppressing hepatitis B (HBV) DNA
- Loss of surface antigen is rare
- OPERA, a large US clinical cohort of people living with HIV (PLWH), has a significant proportion of individuals co-infected with HBV
- Describing individuals who have lost HBV surface antigen and their outcomes could inform HBV cure research

OBJECTIVES

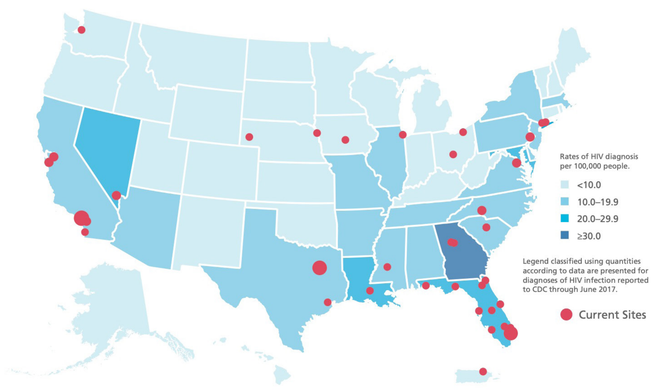
To identify and describe HIV/HBV co-infected individuals who lost HBV surface antigen and their outcomes

Methods

Study population

- The OPERA® cohort (84 clinics in 18 US states/territories) [Figure 1]
- Individuals co-infected with HIV and chronic HBV defined as:
  - HIV diagnosis
  - Prescribed HIV treatment
  - ≥ 2 hepatitis B surface antigen (HBsAg) positive tests after first visit
  - Prescribed HBV treatment
- Excluded those with hepatitis C infection (HCV) at any time during follow up

Figure 1: OPERA locations in the United States overlaying CDC HIV incidence estimates



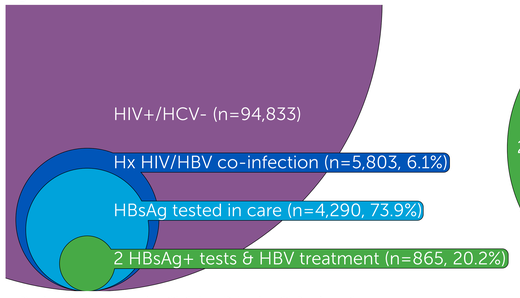
Analyses

- Demographic and clinical characteristics described among:
  - All treated HIV/chronic HBV-coinfected individuals
  - HIV/chronic HBV-coinfected individuals who lost HBsAg at last follow up

Results

- As of July 12, 2019, OPERA followed 105,658 PLWH of which 94,833 did not have HCV during follow up

Figure 2. Study Population



* HBV = hepatitis B virus; HCV = hepatitis C virus; HBsAg = hepatitis B surface antigen

Figure 3. Loss of HBV surface antigen with treatment

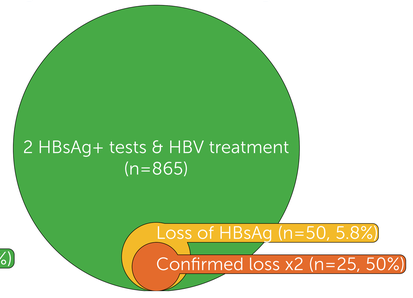


Table 1. Demographic characteristics of HIV/HBV treated individuals with and without loss of surface antigen at last follow-up

Characteristic Median (IQR) or n (%)	No Loss of HBsAg (n=815)	Loss of S HBsAg (n=50)	Confirmed Loss HBsAg (n=25)
Age (years)	50.3 (44.0, 56.0)	46.0 (39.0, 54.6)*	46.5 (44.0, 57.0)
13-25	2 (0.2%)	1 (2.0%)	0
26-49	381 (46.7%)	28 (56.0%)	13 (52.0%)
50+	432 (53.0%)	21 (42.0%)	12 (48.0%)
Female Sex	60 (7.4%)	2 (4.0%)	1 (4.0%)
Black Race	326 (40.0%)	19 (38.0%)	7 (28.0%)
Hispanic Ethnicity	116 (14.2%)	12 (24.0%)	8 (32.0%)*
Region			
Northeast	49 (6.0%)	2 (4.0%)	1 (4.0%)*
South	359 (44.0%)	17 (34.0%)	4 (16.0%)*
Midwest	12 (1.5%)	0	0*
West	395 (48.5%)	31 (62.0%)	20 (80.0%)*
Route of Infection			
MSM	575 (70.6%)	34 (68.0%)*	17 (68.0%)*
IVDU	11 (1.3%)	0*	0*
Both	43 (5.3%)	9 (18.0%)*	6 (24.0%)*
Neither	186 (22.8%)	7 (14.0%)*	2 (8.0%)*

* p-value <0.05 for the comparison with patients without loss of HBsAg
HBV = hepatitis B virus; HBsAg = HBV surface antigen; MSM = men who have sex with men; IVDU = intravenous drug user

Table 2. Testing characteristics of HIV/HBV treated individuals with and without loss of surface antigen at last follow-up

Characteristic Median (IQR) or n (%)	No Loss of HBsAg (n=815)	Loss of S HBsAg (n=50)	Confirmed Loss HBsAg (n=25)
Number of HBsAg tests	2.0 (2.0, 4.0)	5.0 (4.0, 6.0)*	6.0 (5.0, 7.0)*
Time since last HBsAg test	1.7 (1.0, 3.2)	1.6 (0.9, 2.8)	1.9 (0.9, 3.2)*
<1 year	208 (25.5%)	16 (32.0%)	8 (32.0%)
1 to <2 years	256 (31.4%)	15 (30.0%)	6 (24.0%)
2 to <3 years	134 (16.4%)	8 (16.0%)	3 (12.0%)
3 to <4 years	73 (9.0%)	5 (10.0%)	4 (16.0%)
4 or more years	144 (17.7%)	6 (12.0%)	4 (16.0%)
Last HBV VL	110.6 (52.4, 5890.0)	110.6 (19.0, 285.0)	52.4 (19.0, 141.0)*
Undetectable	374 (45.9%)	26 (52.0%)	17 (68.0%)
Detectable <2,000 IU/mL	106 (13.0%)	6 (12.0%)	2 (8.0%)
2,000-20,000 IU/mL	42 (5.2%)	0	0
>20,000 IU/mL	141 (17.3%)	8 (16.0%)	1 (4.0%)
Missing	152 (18.7%)	10 (20.0%)	5 (20.0%)
Time since last HBV VL	1.6 (0.8, 3.6)	2.4 (1.2, 4.2)*	2.7 (1.7, 4.1)*
<1 year	209 (25.6%)	7 (14.0%)	3 (12.0%)
1 to <2 years	181 (22.2%)	9 (18.0%)	3 (12.0%)
2 to <3 years	77 (9.4%)	7 (14.0%)	5 (20.0%)
3 to <4 years	69 (8.5%)	4 (8.0%)	3 (12.0%)
4 or more years	127 (15.6%)	13 (26.0%)	6 (24.0%)
Missing	152 (18.7%)	10 (20.0%)	5 (20.0%)

*p-value <0.05 for the comparison with patients without loss of HBsAg
HBV = hepatitis B virus; HBsAg = HBV surface antigen; HBV VL = HBV viral load

Table 3. Clinical characteristics of HIV/HBV treated individuals with and without loss of surface antigen at last follow up

Characteristic Median (IQR) or n (%)	No Loss of HBsAg (n=815)	Loss of HBsAg (n=50)	Confirmed Loss of HBsAg (n=25)
Duration of OPERA Follow-up (years)	6.5 (3.9, 11.7)	10.7 (6.6, 14.0)*	11.4 (6.6, 16.1)*
<1 year	10 (1.2%)	1 (2.0%)	0
1 to <2 years	44 (5.4%)	2 (4.0%)	0
2 to <3 years	71 (8.7%)	3 (6.0%)	2 (8.0%)
3 to <4 years	80 (9.8%)	2 (4.0%)	2 (8.0%)
4 to <5 years	72 (8.8%)	3 (6.0%)	2 (8.0%)
5 or more years	538 (66.0%)	39 (78.0%)	19 (76.0%)
Duration of HIV Infection (years)	16.8 (9.6, 24.1)	15.4 (8.6, 19.9)	14.0 (8.9, 18.9)
Duration of HBV Infection (years)	6.4 (3.7, 11.2)	7.1 (4.5, 14.0)	7.7 (4.2, 14.0)
Duration of HBV Treatment (years)	5.7 (3.2, 9.3)	9.1 (5.0, 13.6)*	10.0 (6.6, 13.9)*
TDF or TAF ever	655 (82.4)	34 (70.8)	16 (69.6)
Diagnosis of HCC	4 (0.5%)	0	1.0000

*p-value <0.05 for the comparison with patients without loss of HBsAg
HBV = hepatitis B virus; HBsAg = HBV surface antigen; HCC = Hepatocellular carcinoma

Discussion

- Median time to negative HBsAg was 7.3 years (interquartile range [IQR]: 4.6, 14.1); most had been HIV+ for more than 15 years
- All received HBV therapy as part of their HIV therapy; notably, a total of 70 patients were prescribed HIV regimens in which the only anti-HBV agent was lamivudine at last follow-up
- While a substantially higher proportion of those who lost HBsAg were prescribed lamivudine at last follow-up (Loss of HBsAg: n=11, 23%; confirmed loss of HBsAg: n=7, 30%), 81.8% had a history of tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) exposure
- HBV monitoring was infrequent with >17% without HBsAg test in ≥3 years, >23% without HBV VL in ≥3 years and >19% without HBV VL
- Of those with HBsAg loss, median age was 46 (IQR: 40, 54) years, 96% male, 38% black, 23% Hispanic, and 83% men who have sex with men; no statistical difference was observed for these characteristics when compared to those who did not lose HBsAg

KEY FINDINGS

- In this large cohort of HIV/chronic HBV co-infected individuals, loss of surface antigen was observed in 2.9% to 5.8% of patients, which is similar to rates reported in patients with HBV mono-infection
- Monitoring for hepatitis B surface antigen and DNA was lower than expected; efforts are needed to improve recommended monitoring of patients with HBV

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